IT IS CLAIMED:

1. A molecular switch, comprising:
a first nucleic acid construct having
(i) a DNA response element for a transcriptional regulatory protein operably linked to a first promoter;
(ii) a compound binding sequence in the vicinity of said DNA response element for binding to a DNA binding compound;
(iii) a transgene under the control of said first promoter; and
(iv) a DNA binding compound.

2. The molecular switch according to claim 1, further comprising:
(v) a second nucleic acid construct having the coding sequence for a transcriptional regulatory protein operably linked to a second promoter.

3. The molecular switch according to claim 1 or 2, wherein said transcriptional regulatory protein is a native protein.

4. The molecular switch according to claim 2, wherein said transcriptional regulatory protein is a synthetic or engineered protein.

5. The molecular switch according to claim 2, wherein said second promoter is a constitutive promoter.

6. The molecular switch according to claim 2, wherein said second promoter is a regulatable promoter.

7. The molecular switch according to claim 2, wherein a single vector includes said first and second nucleic acid constructs.

8. The molecular switch according to claim 2, having a first vector including said first nucleic acid construct and a second vector including said second nucleic acid construct.

9. The molecular switch according to claim 1, wherein said first nucleic acid construct is an adenovirus vector.

10. The molecular switch according to claim 1, wherein said first nucleic acid construct is an adeno-associated virus vector.

11. A molecular switch, comprising:
a first nucleic acid construct having
(i) a DNA response element for a transcriptional regulatory protein operably linked to a regulatable promoter;

(ii) a compound binding sequence in the vicinity of said transcriptional regulatory protein DNA response element for binding to a DNA binding compound;

(iii) a transgene and the coding sequence for a transcriptional regulatory protein under the control of said regulatable promoter; and

(iv) a DNA binding compound.

12. The molecular switch according to claim 11, further comprising:

(v) the coding sequence for a transcriptional regulatory protein operably linked to said regulatable promoter.

13. The molecular switch according to claim 1 or 11, wherein said nucleic acid construct has from 1 to 12 compound binding sequences.

14. The molecular switch according to claim 1 or 11, wherein compound binding sequence has from about 8 to 20 nucleotides.

15. The molecular switch according to claim 1 or 11, wherein said nucleic acid construct has from 1 to 12 tandem repeated transcriptional regulatory protein DNA response elements.

16. A cell comprising the molecular switch according to claim 1 or 11.

17. A cell according to claim 16, wherein said cell is selected from the group consisting of a plant cell, an animal cell, a yeast cell, a bacterial cell, an insect cell and an archea cell.

18. A method of producing a cell having a molecular switch for modulating gene expression, said method comprising:

(i) transforming said cell with a nucleic acid construct having a DNA response element which binds a transcriptional regulatory protein operably linked to a promoter, a compound-binding sequence in the vicinity of said DNA response element for binding to a DNA binding compound, a transgene under the control of a promoter; and

(ii) exposing said transformed cell to a DNA binding compound,

wherein binding of the DNA binding compound to said compound binding sequence is effective to inhibit binding of a transcriptional regulatory protein to the DNA response element, thereby derepressing or deactivating expression of the gene, where the transcriptional regulatory protein is a repressor or activator protein, respectively.

19. The method according to claim 18, comprising:

(v) further transforming said cell with a second nucleic acid construct having a nucleic acid sequence encoding a transcriptional regulatory protein operably linked to a second promoter.

element is characterized by a series of from 1 to 12 repeated transcriptional regulatory protein binding sites.

28. The cell according to claim 16, wherein said DNA response element is characterized by a series of from 1 to 12 repeated transcriptional regulatory protein binding sites.

29. The molecular switch according to claim 1 or 11, wherein said compound-binding sequence is from about 8 to 20 nucleotides.

30. The cell according to claim 16, wherein said compound-binding sequence is from about 8 to 20 nucleotides.

31. A method of screening DNA binding compounds for the ability to regulate a molecular switch, comprising:

(i) identifying a DNA sequence to which a DNA binding compound is to bind;

(ii) providing a nucleic acid construct having a DNA response element for a transcriptional regulatory protein and a compound binding sequence in the vicinity of said DNA response element; and

(iii) screening a plurality of candidate DNA binding compounds, by exposing each of the candidate compounds to said nucleic acid construct
and identifying DNA binding compounds having the ability to bind to the compound-binding sequence.

32. The method according to claim 31, further comprising:

(iv) combining a transcriptional regulatory protein with said nucleic acid construct, and identifying and selecting DNA binding compounds having the ability to bind to displace said transcriptional regulatory protein from said DNA response element.

33. The method according to claim 32, further comprising:

(v) modifying said nucleic acid construct to further include a transgene under the control of a promoter, wherein said transgene is a reporter gene, and identifying and selecting DNA binding compounds having the ability to inhibit binding of said transcriptional regulatory protein to said DNA response element, as evidenced by derepression or deactivation of expression of the reporter gene, where the regulatory protein is a repressor or activator protein, respectively.

Add D7

20. A method of modulating expression of an exogenous gene in a cell by a DNA binding-compound, comprising:

adding said DNA binding-compound to a cell which expresses a transcriptional regulatory protein, and is transformed with a genetic construct having a DNA response element which binds said transcriptional regulatory protein operably linked to a promoter, a compound-binding sequence in the vicinity of said DNA response element for binding to said compound, and a transgene under the control of said promoter,

wherein addition of said DNA binding compound to said cell, and binding of the compound to said compound-binding sequence is effective to inhibit binding of said transcriptional regulatory protein to the DNA response element, thereby derepressing or deactivating expression of the exogenous gene, where the transcriptional regulatory protein is a repressor or activator protein, respectively.

21. The molecular switch according to claim 1 or 11, wherein said transcriptional regulatory protein has a DNA binding sequence selected from the group consisting of a UL9 sequence, an NF-κB sequence, a GAL4 sequence, a ZFHD1 sequence, a LacR sequence, a TetR sequence, a LexA sequence, and the ecdysone receptor binding sequence.

22. The cell according to claim 16, wherein the DNA binding sequence of said transcriptional regulatory protein is selected from the group consisting of a UL9 sequence, an NF-κB sequence, a GAL4 sequence, a ZFHD1 sequence, a LacR sequence, a TetR sequence, a LexA sequence, and the ecdysone receptor binding sequence.

23. The molecular switch according to claim 1 or 11, wherein said regulatory domain is an activator domain selected from the group consisting of VP16, NF-KB, Gal4, TFE3, ITF1, Oct-1, Sp1, Oct-2, NFY-A, ITF2, c-myc, and CTF.

24. The cell according to claim 16, wherein the regulatory sequence of said of said transcriptional regulatory protein is an activator selected from the group consisting of VP16, NF-KB, Gal4, TFE3, ITF1, Oct-1, Sp1, Oct-2, NFY-A, ITF2, c-myc, and CTF.

25. The molecular switch according to claim 1 or 11 wherein the regulatory sequence of said of said transcriptional regulatory protein is a repressor selected from the group consisting of Kruppel (KRAB), kox-1, TetR, even-skipped, LacR, engrailed, hairy (HES), Groucho (TLE), RING1, SSB16, SSB24, Tup1, Nab1, AREB, E4BP4, HoxA7, EBNA3, Mad and v-erbA.

26. The cell according to claim 16, wherein the regulatory sequence of said of said transcriptional regulatory protein is a repressor selected from the group consisting of Kruppel (KRAB), kox-1, TetR, even-skipped, LacR, engrailed, hairy (hes), Groucho(TLE), RING1, SSB16, SSB24, Tup1, Nab1, AREB, E4BP4, HoxA7, EBNA3, Mad and v-erbA.

27. The molecular switch according to claim 1 or 11, wherein said DNA response